***Hyperemesis gravidarum and thyroid disease***

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Nausea and vomiting are common symptoms in early pregnancy, affecting 70-80% of pregnant women, usually started 5-6 weeks gestation and relieved by 12-14 weeks, 90% have no symptoms by 16 weeks. Hyperemesis is less common and causes serious morbidity.

***Hyperemesis gravidarum***: is defined as vomiting sufficiently severe to produce weight loss (>5% of pre pregnancy weight), dehydration, alkalosis from loss of hydrochloric acid, and hypokalemia. Acidosis develops from partial starvation, in some patients transient hepatic dysfunction develops.

Severe hyperemesis requiring hospital admission occurs in 0.3-2% of pregnancies associated with an increased risk of preterm birth and low birthweight babies

**Incidence:** It appears to be related to high or rapidly rising serum levels of pregnancy-related hormones possibly: human chorionic gonadotropin (hCG) and estrogens. However it is more common in:

1.primigravida

2.multiple gestation

3.history of previous hyperemesis and motion sickness

4.molar pregnancy

5.a female fetus

6.younger women

7.obese women

8. An association of *H. pylori* infection has been proposed.

9.ethnic predisposition and family history

**Clinical presentation*:***

***Signs and symptoms***:

-Excessive nausea and vomiting in early pregnancy

- Excessive salivation (ptylism) in 60%

- Dehydration (dry and coated tongue, inelastic skin, sunken eye, postural changes in blood pressure and pulse rate)

- Significant weight loss, jaundice, metabolic acidosis.

***Complications:***

***Maternal:***

1. Vomiting may be prolonged, frequent, and severe causing:

Mallory-Weiss tears—bleeding, pneumothorax, pneumomediastinum and esophageal rupture.

2. Depression that could be a cause or effect.

3. Wernickes encephalopathy: CNS dysfunction due to deficiency in thiamine B1 presents with apathy, confusion, ataxia and blindness. long-term sequelae are common and include blindness, convulsions and coma. A third of women have an abnormal electroencephalogram (EEG).

4. Various degrees of acute renal failure from dehydration are encountered that may require dialysis.

5. Hypoprothrombinemia—vitamin K deficiency causing maternal coagulopathy and fetal intracranial hemorrhage

6. Central pontine mylenolysis, acute peripheral neuropathy and maternal death.

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***Fetal:***

If there is maternal weight loss more than 10% then poor fetal outcome in form of fetal growth restriction and fetal death is expected.

**Diagnosis:**

A pregnant woman presents with excessive nausea and vomiting. The **diagnosis of hyperemesis is by exclusion** of other causes of nausea and vomiting which could be: (***DDX***)

**Gastrointestinal**: peptic ulcer, gastroenteritis and pancreatitis.

**Genitourinary**: pyrlonephritis, renal stone and leiomyoma red degeneration.

**Metabolic**: diabetic ketoacidosis and hyperthyroidism.

**Neurological**: tumours and meningitis

**Others**: poisoning, psychological and fatty liver of pregnancy.

***Investigations:***

1. Ultrasound to confirm the pregnancy and exclude twin and molar pregnancy.

2. GUE for ketones( which indicates dehydration) and infection

3. Complete blood count: hemoconcentration (raised PCV)

4. Renal function test: raised urea and creatinine

5. Liver function test: increased bilirubin and transaminases, virology screen.

6. Thyroid function test: raised T4 and suppressed TSH

7. Raised serum amylase.

8. Electrolytes: decreased Na, K , Cl

9. Metabolic alkalosis and later acidosis due to starvation.

**Treatment:**

1. Small liquid meals are better tolerated than solid, less nausea with protein meals than carbohydrates and fat.

2. Psychological support and home environment changes.

3. **Indications for admission**: If vomiting persists after rehydration and failed outpatient management, severe dehydration, electrolyte abnormalities, acidosis, infection, significant wt loss and if there is doubt about the diagnosis.

4. Fluid therapy***(the most important)***: ringer solution is a good choice, normal saline 1 L+ 20-40 mmol KCL 8-hourly. Dextrose is better to be avoided as it may precipitate Wernicke's encephalopathy. Continue the fluid until the patient can take oral fluid and no ketones in urine.

5. Vitamine therapy: B6 10-30mg per day is safe and reduces the nausea

Thiamine orally 25-50mg or IV 100mg weekly

6. Anti-emetic therapy: are safe in pregnancy, antiemetics such as cyclizine 50mg , promethazine 25mg, chlorpromazine 10mg or metoclopramide 10mg are given orally or parenterally 2-3 times\d.

7. Steroids: there is little evidence that treatment with *glucocorticosteroids* is effective.

8. Nutritional Support: in the small percentage of women who continue to have severe vomiting, consideration is given for enteral or parenteral nutrition

**Thyroid disorders:**

In pregnancy there is altered thyroid binding globulin as a result of increased estrogen which increases its synthesis, as a result there is increased level of total T3 and T4 but the free portion is unchanged. So it is important to measure the free T3 and T4 and to base the management on these levels, the lower limit of normal of free T4 is below that of non pregnant.

There is iodine deficiency as a result of loss through increased GFR. This results in increased uptake by thyroid gland that results in goiter.

**Hyperthyroidism**:

It occurs in 1:500 pregnancies

***Causes***: most of cases are due to Graves' disease which is an autoimmune disorder with high levels of circulating thyroid stimulating antibodies. Other causes (<5%) are: toxic nodule, thyroiditis, multinodular goiter, carcinoma and rarely trophoblastic disease.

The diagnosis may be difficult to make in pregnancy because maternal tachycardia, wt loss, heart murmurs and heat intolerance are common symptoms in pregnancy.

Women with well-treated disease rarely have maternal complications

of pregnancy, Poorly controlled hyperthyroidism is associated with several **pregnancy complications**, including: cardiac arrhythmias, maternal thyrotoxic crisis, miscarriage, gestational hypertension, pre-eclampsia, preterm labour, diarrhea, abdominal pain and psychosis.

Thyroid stimulating antibody may cross the placenta and cause fetal hyperthyroidism and goiter which may obstruct labour. Other fetal complications are: fetal tachycardia, prematurity and intrauterine growth restriction. The risk of these complications is reduced if the disease is adequately controlled before delivery.

**Investigations**:

Hyperthyroidism is confirmed by elevated FT3, FT4 and reduced level of TSH.

**Treatment:**

1. Antithyroid drugs: The principal drugs used to treat hyperthyroidism (propylthiouracil and carbimazole) which inhibit thyroid hormone synthesis, there is no evidence that either drug is associated with congenital abnormalities. Both drugs may rarely cause neutropenia and agranulocytosis. Therefore patients should be aware that symptoms of infection, particularly sore throat, may be associated with bone marrow suppression and they must have a neutrophil count checked immediately should they occur. Once drug treatment has been commenced thyroid function tests should be carried out and checked regularly, the aim is to maintain maternal FT3 and FT4 in the high normal range and the lowest dose of drug must be used as propylthiouracil and carbimazole both cross the placenta. However, fetal hypothyroidism is rarely seen.

Women requiring antithyroid medication should not be discouraged from breastfeeding. They should be encouraged to feed before taking the medication and to take divided doses.

2. Beta blockers may be indicated to control the arrhythmias

3. Surgery is rarely indicated when there is no response to medical treatment, pressure effect of goiter and suspicion of malignancy. There is a risk of thyrotoxic crisis, also called ‘thyroid storm’, is a medical

emergency that can present with exaggerated features of hyperthyroidism in addition to hyperpyrexia, congestive cardiac failure, dysrhythmias and an altered mental state. It may be precipitated by infection, abrupt cessation of treatment, surgery, labour or delivery and must be

treated immediately as it can be life threatening. Treatment involves administration of intravenous fluids, hydrocortisone, propranolol, oral iodine and carbimazole or propylthiouracil.

Radioactive iodine is contraindicated because it completely obliterates the fetal thyroid gland.

**Hypothyroidism**

It affects approximately 1% of pregnant women. Providing thyroxine replacement therapy is adequate, hypothyroidism is not associated with an adverse pregnancy outcome for the mother or fetus. An association between poorly controlled hypothyroidism and a variety of adverse outcomes, including: congenital abnormalities, hypertension, premature delivery, fetal growth restriction , placental abruption and post-partum haemorrhage.

Overt hypothyroidism causes subfertility, and the presence of thyroid

autoantibodies, even if the mother is euthyroid, is associated

with an increased risk of miscarriage . Severe hypothyroidism affects the subsequent intelligence of the offspring of affected mothers with neurodevelopmental delay at the age of 7–9.

**Causes:**

The commonest cause is iodine deficiency which may result in cretinism of the newborn as a result of congenital hypothyroidism; other is autoimmune hashimoto's thyroiditis.

**Treatment:**

Women with hypothyroidism should be given thyroxine replacement at a dose that ensures their thyroid function tests are normal with a FT4 at the upper end of the normal range appropriate for each trimester of pregnancy. Thyroxine is best taken on an empty stomach and 4 h apart from any iron or other supplements

**Post-partum thyroiditis**

Post-partum thyroiditis is associated with the presence of thyroid antiperoxidase antibodies. The incidence varies between 2 and 16%. It is characterized by an initial hyperthyroid phase that classically occurs

1–3 months post-partum, followed by a hypothyroid phase, which usually resolves by 12 months after delivery.

The hypothyroidism may require treatment with thyroxine, but treatment should be stopped after 1 year as many cases resolve. However, there is a risk of developing subsequent hypothyroidism in women who have

had post-partum thyroiditis, so affected women should have their thyroid function checked regularly.

**Pituitary disorders:**

Hyperprolactinaemia in pregnancy is mostly due to microadenoma treated with bromocriptine and cabergoline which are dopamine agonists.

Other causes are: drugs, macroadenoma or disconnecting tumour in hypothalamic reigon which might need surgery or radiotherapy which is best undertaken before pregnancy.

For microadenoma the treatment is usually stopped during pregnancy, it may enlarge during pregnancy but rarely cause a problem, with frequent monitoring of visual field, if tumour enlarges then treatment is recommended.

For macroadenoma (>1cm size) it is best to continue with dopamine agonist because the risk of tumour enlargement, there is no evidence that drugs are teratogenic.

**Adrenal disorders**:

All adrenal diseases are rare in pregnancy

**Cushing syndrome**:

It characterized by increased glucocorticoid production due to adrenal or pituitary causes.

Most females are infertile, if get pregnant then high incidence of preterm delivery and still birth.

The diagnosis is difficult because the symptoms mimic normal pregnancy changes as striae, weight gain, weakness, hypertension and diabetes.

Assay of plasma cortisol, CT, US, MRI are indicated.

**Addison disease**:

Presents with exhaustion, hypotension, hypoglycemia and wt loss

Occasionally may present with crisis which is treated with fluid and glucocorticoid

Treatment: replacement with steroids should continue during pregnancy with parenteral therapy at time of stress such as labour

**Phaeochromocytoma:**

Is rare presents with hypertensive crisis like preeclampsia, characteristic feature is paroxysmal hypertension, other features as headache, blurring of vision, anxiety and convulsion.

Diagnosis: measurement of the level of catecholamines

Treatment: alpha blockers and phentolamine, preferably delivery by caesarean section to avoid the sudden increase in catecholamines associated with delivery.

End of lecture